Exhibit I

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similar (RP median 2·8 *v* IRA 2·2/annum). During a median 6·5 years of follow up IRA patients required, on average, one admission for fulguration. Before surgery RP patients passed more stools/24 h (median RP 4 *v* IRA 2, p<0·001). Postoperative rates were four and three respectively. Night defecation was commoner after RP (41% *v* 10%, p=0·001) but more RP patients could delay defecation for 15 minutes (79% *v* 50%, p=0·02). Although more RP patients used constipating medication (30% *v* 17%) and noted anal leakage (41% *v* 28%) these differences were not statistically significant. Of RP patients 14% catheterised regularly; all were operated upon over five years ago.

IRA causes less morbidity. Restorative proctocolectomy patients' less satisfactory bowel function is the result of patient selection as well as the operation itself.

Does faecal urgency and incontinence relate to rapidity of rectal filling?

C S DUTHIE, ANN MILLS, AND D C C BARTOLO (*University of Bristol, Department of Surgery, Bristol Royal Infirmary, Bristol*) It has been suggested that urgency and associated faecal incontinence may be related to rapid rectal filling from more proximal colon. Sixteen incontinent patients (INC) were investigated by proctometrography at a standard (STD) 60 ml/min filling speed and at a speed of 150 ml/min (FAST) to determine if filling rate altered first reactal appreciation, maximum tolerable volume or pressure, or rectal compliance, and these were compared with out control group of 12 subjects (C). Ages in both groups were comparable (C=55 median (24–83 range); INC 50 (29–81)). First appreciation of rectal filling was not affected by filling rate (STD=60 ml 38–160); FAST=55 (25–110):NS*) and was no different from controls (67·5 (35–145)†). Similarly, maximum tolerable volume was unaltered (STD=185 ml (85–380); FAST=185 115–370):NS*) as was maximum tolerable pressure (STD 120 cmH20 (85–170); FAST=115 (70–190):NS*). Rectal compliance was not significantly altered at either speed SDT=2·25 ml/cmH20 (0·6–4·4); FAST=2·4 0·8–4·8):NS*) nor reduced when compared with controls (4·60 (2·25–7·9):NS†).

We conclude feelings of urgency, or urge incontinence are not related to rate of rectal filling nor altered rectal appreciation of filling in incontinent patients.

*Wilcoxon signed ranked pairs test: †Mann-Whitney U test.

Internal anal sphincter electromyographic frequency is related to anal canal resting pressure. Both are reduced in idiopathic faecal incontinence

C S DUTHIE, R MILLER, AND D C C BARTOLO (*University of Bristol, Department of Surgery, Bristol Royal Infirmary, Bristol*) Previous studies have not shown a relationship between the internal anal sphincter electromyogram (IASEMG) and resting anal canal pressures (RP). We have investigated RP (air filled manometry) and IASEMG, frequency and amplitude changes (frequency cut offs 0·1–15 Hz) in five controls (C), nine patients with idiopathic faecal incontinence (IFI) and 10 with slow transit constipation (STC) to elucidate IASEMG changes associated with these disorders. Resting anal pressure (C=80 cmH20 median (40–105 range); IFI=45 (20–65); STC=75 (45–150)) was reduced in IFI *v* controls (p<0·05) and STC (p<0·001), but STC and controls were similar. There were no differences in any groups for IASEMG Amplitude (c=60 mV (40–120); IFI=60 (20–140); STC=91 (40–148)). But IASEMG frequency changes (C=0·41 Hz (0·25–0·5); IFI=0·25 (0·19–0·45); STC=0·38 (0·25–0·55)) were significantly reduced in IFI *v* Controls (p<0·05) and STC (p<0·01) but not between STC and Controls. In fact, considering all 24 subjects results RP (60 (20–150)) correlated well with IASEMG frequency (0·34 Hz (0·19–0·55): r=0·87, p<0·001) but not with IASEMG amplitude (66 mV (20–148): r=0·31, p>0·05).

We conclude IASEMG frequency changes relate to anal resting pressure changes and that low pressures seen in IFI are related to low IASEMG activity. Slow transit constipation is not related to increased sphincter activity.

BASIC SCIENCE

Monoclonal antibody C242 recognises a tumour associated antigen in colorectal carcinomas

N ROTHNIE, H SU N ROONEY, E DANKWA, C WOOD, AND N HABIB (*Department of Surgery, Royal Postgraduate Medical School, London and Department of Histopathology, Bristol Royal Infirmary*) C242 is a murine monoclonal antibody (IgG2) raised after immunisation with Colo 205, a human colonic adenocarcinoma cell line. It binds to a sialated carbohydrate structure, CA 242, closely related to CA 19–9 and CA 50. The aim of this study was to assess the immunohistochemical reactivity of C242 in normal and diseased colonic tissues.

Formalin fixed, paraffin embedded tissue sections were stained with C242 using the avidin biotin peroxidase method. Three observers assessed the percentage of cells showing positive staining and the cytological distribution of staining. Eighty five per cent (38/45) of the colonic carcinomas, 87% (13/15) of colonic lymph node metastases and 63% (five of eight) of colonic liver metastases showed strong positive staining. Staining was localised to the supranuclear cytoplasm, cell membrane and superficial mucin, and was not related to Dukes stage or histological grade of the tumour. Only 14% (four of 28) of the sections of normal colonic mucosa and 11% (four of 37) of normal mucosa adjacent to tumours showed slight positive staining. No staining was seen in normal liver (eight) or lymph nodes (10), and little or no staining was seen in a wide range of other normal tissues.

These data suggest that C242 recognises a tumour associated antigen which is expressed by colonic carcinomas. C242 may be of further use in immunodiagnosis and immunotherapy of colorectal carcinomas.

Acyclovir and 2', 3'-dideoxycytidine treatment of duck hepatitis B virus infected Aylesbury ducks: use of free and liposome entrapped drugs

G VARAGONA, I. ELLIS, H DASILVA, D MOORE, G GREGORIADIS, P J SCHEUER, AND G DUSHEIKO (*Department of Medicine, Royal Free Hospital, London NW3 2QG*) The duck hepatitis B virus (DHBV) model is a useful *in vivo* system for the evaluation of the efficacy of antiviral drugs in the treatment of hepadnavirus virus infection. We are currently investigating the efficacy of antiviral agents in this model together with the possibility of using liposomes as a targeting system. Fifteen chronically infected Aylesbury ducks were investigated. Group A were given 5 mg/kg/day free acyclovir, group B 5 mg/kg/day liposome entrapped ACV; group C 5 mg/kg/day free 2', 3'-dideoxycytidine (DDC), group D 5 mg/kg/day liposome entrapped DDC; group E were controls, injected with empty liposomes. Both drugs were injected iv twice a day for five days. The efficacy of the treatment was evaluated by measuring DHBV-DNA in the serum by molecular hybridisation. In all the ducks of group A and B serum DHBV-DNA became negative within two days of treatment, while only slight fluctuations were observed in the ducks treated with DDC. In all responder ducks DHBV-DNA became detectable again within three days after stopping the therapy. No changes were observed in the control ducks. No significant histopathological modifications were noted as a consequence of the treatment. Acyclovir appears to exert a potent inhibitory effect on DHBV replication when administered both in a free and in a liposome entrapped formulation. On the contrary, DDC seems to have low efficacy. The acyclovir results provide a rationale for attempting dose reductions when the drug is administered in a liposome entrapped preparation.

Identification of an immunodominant 57 kDa *Giardia lamblia* antigen

S CHAR, N SHETTY, M NARASIMHA, E ELLIOTT, R MACADEN, AND M J G FARTHING (*Department Gastroenterology, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE and Department of Microbiology, St John's Medical College, Bangalore, India*) The identification, cloning and characterisation of immunodominant *Giardia* antigens is essential for functional studies of immunity, for improving serodiagnostic tests and selection of protective antigens in vaccine development. We have investigated the antibody responses to specific *Giardia* antigens by subjecting trophozoites to SDS-PAGE followed by Western blotting and probing with sera from 10 children with giardiasis (0·5–5 yr) from South India and 10 age matched controls from the same area. A band corresponding to 57kDa was recognised by IgG and IgA antibodies in sera of all 10 patients and none of the controls. The protein nature of the 57kDa antigen was demonstrated by loss of antibody recognition after trypsinisation. Subcellular fractionation of trophozoites followed by SDS-PAGE and immunoblotting showed that the 57kDa antigen was not a cytoskeletal protein such as tubulin. We have produced a mouse monoclonal antibody (Mab) by immunising mice with whole *Giardia* trophozoites which identifies a non-cytoskeletal antigen molecule of 57kDa. Indirect immunofluorescence with the Mab confirms that this is predominantly a cytosolic protein with some surface expression. We are currently screening a *Giardia lamblia* expression library for the gene which encodes the 57kDa antigen. The immunological and functional significance of this protein remains to be determined.